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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,041	01/09/2001	John C. Reed	P-LJ 4494	6395

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EXAMINER
UNGAR, SUSAN NMN

ART UNIT	PAPER NUMBER
1642	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/757,041	Reed et al
Examiner	**Art Unit**
Ungar	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 20, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *13-34* is/are pending in the application.

4a) Of the above, claim(s) *16-18, 22, 26, 27, and 31-33* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *13-15, 20, 21, 23-25, and 28-30* is/are rejected.

7) ☒ Claim(s) *19 and 34* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Election filed August 20, 2002 (Paper No. 11) in response to the Office Action of July 22, 2002 (Paper No. 10) is acknowledged and has been entered. Claims 13-34 are pending in the application and Claims 16-18, 22, 26, 27, 31-33 has been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 13-15, 19-21, 23-25, 28-30, 34 are currently under prosecution.

2. The response (Paper No. 11) to the Letter of July 22, 2002 (Paper No. 10) has been received. Applicant has elected Group VII, claims 13-21 and 23-34, drawn to a method of identifying an effective agent that alters the association of CAP and a second molecule *in vitro* by decreasing association for examination with traverse and incorporate by reference the remarks set forth in the Response (submitted June 4, 2002, Paper No.9) to the Restriction Requirement mailed May 25, 2002 (Paper No. 7) and requests that the traversal be fully considered. Applicant reiterates, with traverse, the election of species of CD40 as the second molecule, yeast cell as the cell and a drug as the agent.

In Paper No. 9, Applicant argues that (a) the search and examination of claims 13-34 as a whole does not pose a serious burden on the examiner, (b) that in the parent case, claims 13-34 were grouped together and no species requirement was made, (c) all of the subject matter within groups IV-VII is classified in the same class and subclass. The arguments have been considered but have not been found persuasive because (a') the literature search, particularly relevant in this art, is not coextensive, (b') although the previous Examiner grouped claims 13-34 together, upon review and reconsideration, Examiner found that the identified groups and

species were distinct for the reasons set forth in Paper No. 7, (c') classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

3. The specification on page 1 should be amended to reflect priority claimed to the parent application and also to reflect the status of the parent application.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

5. Claims 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth CAP-1, SEQ ID NO:1 which associates with the cytoplasmic domain of CD40 and therefore the written description is not commensurate in scope with the claims drawn to a method of

identifying an effective agent that alters the association of a CAP with a CD40 in a yeast cell, in a mammalian cell.

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The specification teaches that the ligand for CD40 is CD40L (p. 7, line 11). The specification teaches that how CD40 transduces its CD40L-binding signal into a B cell is unknown. Since CD40 is present on the cell surface, its action likely is mediated by CD40 binding to one or more intracellular proteins. However, the cytoplasmic domain of CD40 provides no clues as to how intracellular signaling is accomplished since the domain lacks homology to kinases or other enzymes known for mediating intracellular signaling (p.2, lines 25-35). The specification further teaches that the identification of intracellular proteins that can associate with CD40 and transduce the CD40L-binding signal into a cell would provide a means to manipulate various cellular functions. Thus a need exists to identify proteins that associate with CD40. The present invention satisfies this need (p. 3, lines 1-8). The specification further discloses an isolated cDNA sequence, SEQ ID NO: 2, which encodes a polypeptide sequence, SEQ ID NO. 1 (CAP-1) which associates with the cytoplasmic domain of CD40. CAP-1 was isolated and identified using the yeast two hybrid system (see Example 1). Of the 166 clones tested, two clones were found that reacted with CD40, but not other fusion proteins (p. 46) and it was shown that the two clones contained identical cDNA inserts suggesting that the two

clones arose as library-amplified copies of a single cDNA. The cDNA was named CAP-1 (p. 46). The encoded protein was shown to bind CD40 in a cell lysate and to bind to GST CD40 fusion protein (p. 49) and it appears that CAP-1 precipitates with CD40 in Western blots from lymphoma cell lysates (p. 50). The specification goes to on disclose a prophetic experiment for screening a cDNA expression library for other intracellular CAPs (p. 51-p. 53). It is noted that the specification does not teach that any CAP associates with any molecule other than CD40.

The instant disclosure of a single species of polypeptide that associates with CD40 intracellularly does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of undefined subgenera. Although drawn to cDNA, the findings in *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) are relevant to the instant rejection. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polpeptides. The specification discloses that the cytoplasmic domain of CD40 provides no clues as to how intracellular signaling is accomplished since the domain lacks homology to kinases or other enzymes known for mediating intracellular signaling, thus it cannot be predicted what structures would be required in order to bind to the cytoplasmic domain. The specification hypothesizes that "one or more

intracellular proteins" likely mediate the actions by CD40 binding to CD40L (p. 2, lines 25-30). Thus it is clear that at the time the invention was made, Applicant did not know whether there was more than one CAP. Certainly, in the cell type from which CAP-1 was isolated, there does not appear to be any CAP other than CAP-1. Further, there is no description of the conserved regions which are critical to the structure and function of the genus claimed. The specification proposes to discover other members of the genus by using the yeast two-hybrid system. Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity, that is by associating with CD40, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In addition, there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed and no identifying characteristic or property of the instant

polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is undefined other than by CAP-1, the disclosure of a single polypeptide sequence and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Therefore only a method a method of identifying an effective agent that alters the association of a CAP-1, SEQ ID NO:1 with CD40 in a yeast cell, in a mammalian cell., but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 13-15, 20-21, 25, 28-30 are rejected under 35 U.S.C. § 102(b) as being anticipated by Noelle et al (PNAS, 1992,89:6550-6554, IDS item) as evidenced by Foy et al (J. Exp. Med., 1993, 178:1567-1575, IDS item).

It is assumed for examination purposes that, as defined by the specification, a "CAP" is a protein that binds specifically to CD40 (p. 5, lines 4-10).

Foy et al teach that anti-gp39 antibody, MR1 has profound immunosuppressive effects on humoral immunity by blocking gp 39-CD40 interactions *in vivo* (abstract and Fig 1).

In the absence of a definition for a "drug" within the specification, it is assumed for examination purposes that the term "drug" is meant to have an art recognized definition, that is, a drug is any substance that, when taken into a living organism may modify one or more of its functions (see Taber's Cyclopedic Medical Dictionary, 16th Ed., F.A. Davis Co., Philadelphia, 1989, p. 534). It is noted that by art-recognized definition, antibody MR1 is a drug.

The claims are drawn to a method of identifying an effective agent that alters the association of a CAP with a second molecule comprising contacting the CAP with a second molecule, CD40, adding an agent and detecting whether association of CAP with CD40 is decreased *in vitro*, wherein the cell is a mammalian cell, the agent is a drug, wherein said altered association is detected by measuring the transcriptional activity of a reporter gene.

Noelle et al (PNAS, 1992,89:6550-6554) teach a method of identifying an effective agent (anti 39-kDa antibody, MR1) that alters the association of a CAP (gp39 on activated T_h cell plasma membrane) with a second molecule, CD40 (see abstract) comprising contacting the CAP and a second molecule, CD40 on B cells, adding an agent, MR1 anti-39-kDa antibody (p. 6553, cols 1 and 2) to the mixture wherein T_h cell plasma membrane B-cell activation was inhibited, wherein altered

association was assayed by the effects of MR1 on B-cell RNA synthesis by the activated plasma membranes, wherein MR1 significantly inhibited the induction of B-cell RNA (see Figure 6, page 6553, col 2). Although the reference does not specifically state that MR1 alters the association of CAP and CD40, the claimed method appears to be the same as the prior art method absent a showing of unobvious differences. The office does not have the facilities for examining and comparing applicant's method with the method of the prior art in order to establish that the method of the prior art does not possess the same material structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed method is functionally different than that taught by the prior art and to establish patentable differences. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat.
App. & Int.).

Claim Objections

8. Claims 19 and 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
October 14, 2002